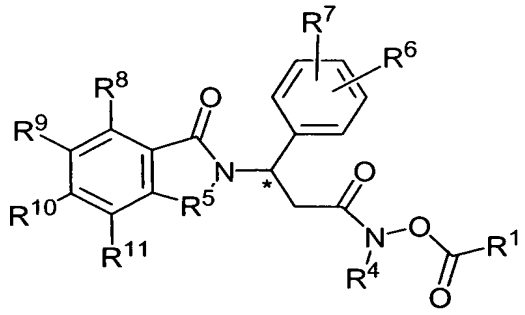
Amendments to the Claims

The following listing of claims will replace all prior versions and listings of claims in this application.

1. (Currently amended) ~~An acylhydroxamic acid derivative, selected from the group consisting of~~A pharmaceutical composition comprising:

(a) a ~~compounds~~ compound of the formula:



or an acid addition salts thereof,

wherein

the carbon atom designated * constitutes a center of chirality,

R^4 is hydrogen or -(C=O)-R^{12};

each of R^1 and R^{12}, independently of each other, is alkyl of 1 to 6 carbon atoms, phenyl, benzyl, pyridyl methyl, pyridyl, imidazoyl, imidazolyl methyl, or

$CHR^*(CH_2)_nNR^*R^0$

wherein $R^*$and R^0, independently of the other, are hydrogen, alkyl of 1 to 6 carbon atoms, phenyl, benzyl, pyridylmethyl, pyridyl, imidazoyl or ~~imidazolylmethlyl~~ imidazolylmethyl, and n = 0, 1, 2;

R^5 is C=O, CH_2, ~~CH2-CO-~~ -CH_2-CO-, or SO_2;

each of R^6 and R^7, independently of the other, is nitro, cyano, trifluoromethyl, carbethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxy, carboxy, hydroxy, amino, alkyl of 1 to 6 carbon atoms, alkoxy of 1 to 6 carbon atoms, cycloalkoxy of 3 to 8 carbon atoms, halo, bicycloalkyl of up to 18 carbon atoms, tricycloalkoxy of up to 18 carbon atoms, 1-

indanyloxy, ~~2indanyloxy~~ 2-indanyloxy, C_4-C_8-cycloalkylidenemethyl, or C_3-C_{10}-alkylidenemethyl; and

each of R^8, R^9, R^{10}, and R^{11} independently of the others, is

(i) hydrogen, nitro, cyano, trifluoromethyl, carbethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxy, carboxy, hydroxy, amino, alkylamino, dialkylamino, acylamino, alkyl of 1 to 10 carbon atoms, alkoxy of 1 to 10 carbon atoms, halo, or

(ii) one of R^8, R^9, R^{10}, and R^{11} is acylamino comprising a lower alkyl, and the remaining of R^8, R^9, R^{10}, and R^{11} are hydrogen, or

(iii) hydrogen if R^8 and R^9 taken together are benzo, quinoline, quinoxaline, benzimidazole, benzodioxole, 2-hydroxybenzimidazole, methylenedioxy, dialkoxy, or dialkyl, or

(iv) hydrogen if R^{10} and R^{11}, taken together are benzo, quinoline, quinoxaline, benzimidazole, benzodioxole, 2-hydroxybenzimidazole, methylenedioxy, dialkoxy, or dialkyl, or

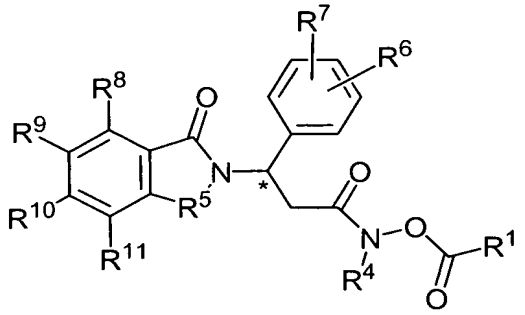
(v) hydrogen if R^9 and R^{10} taken together are benzo; and

(b) ~~The acid addition salts of said compounds which contain a nitrogen atom capable of being protonated~~ a pharmaceutically acceptable carrier.

Claims 2-4. Cancelled

5. (Currently amended) ~~An acylhydroxamic acid derivative~~ A pharmaceutical composition comprising:

(a) a compound of the formula ~~according to claim 1 wherein said compound has the formula~~:



or an acid addition salt thereof,

in which

the carbon atom designated * constitutes a center of chirality;

R^4 is hydrogen or -(C=O)-R^{12}, where

each of R^1 and R^{12}, independently of each other, is alkyl of 1 to 6 carbon atoms, phenyl, benzyl, pyridyl, pyridyl methyl, imidazolyl, imidazoylmethyl, or $CHR^*(CH_2)_nNR^*R^0$

wherein $R^*$and R^0, independently of the other, are hydrogen, alkyl of 1 to 6 carbon atoms, phenyl, benzyl, pyridylmethyl, pyridyl, imidazoyl or imidazolylmethlyl, and n = 0, 1, 2;

R^5 is C=O or CH_2;

each of R^6 and R^7, independently of the other is alkoxy of 1 to 8 carbon atoms, cycloalkoxy of 3 to 6 carbon atoms.; ~~C_4-C_6-cycloAlkylidenem ethyl~~ C_4-C_6-cycloAlkylidenemethyl, ~~C_2-C_{10}alkylidenemethyl~~ C_2-C_{10}-alkylidenemethyl, C_6-C_{18}-bicycloalkoxy, C_6-C_{18}-tricycloalkoxy, 1-indanyloxy, or 2-indanyloxy; ~~and~~

each of R^8, R^9, R^{10}, and R^{11}, independently of the others, is hydrogen, nitro, cyano, trifluoromethyl, carbethoxy, carbomethoxy, carbopropoxy, acetyl, halo, carbamoyl, acetoxy, carboxy, hydroxy, amino, alkylamino, dialkylamino, acylamino, alkyl of 1 to 10 carbon atoms, and alkoxy of 1 to 10 carbon atoms; and

(b) a pharmaceutically acceptable carrier.

Claims 6-18. Cancelled

19. (Currently amended) The pharmaceutical composition ~~comprising a quantity of an acylhydroxamic acid derivative according to~~ of claim 1, ~~which derivative~~wherein said compound is a substantially chirally pure (R)-isomer, a substantially chirally pure (S)-isomer, or a mixture thereof, ~~sufficient upon administration in a single or multiple dose regimen to~~ and wherein the composition is useful for ~~reduce~~ reducing or ~~inhibit~~ inhibiting levels of TNFα, ~~or~~ PDE 4 or a matrix metalloproteinases in a mammal ~~in combination with a carrier~~.

20. Cancelled.

21. (Currently amended) A method of inhibiting the ~~undesirable~~ levels of TNFα in a mammal which comprises administering thereto ~~an effective amount of an acylhydroxamic acid derivative~~ a pharmaceutical composition according to claim 1, wherein said compound ~~which derivative~~ is a substantially chirally pure (R)-isomer, a substantially chirally pure (S)-isomer, or a mixture thereof.

22. (Currently amended) A method of inhibiting the ~~undesirable~~ levels of matrix metalloproteinases in a mammal which comprises administering thereto ~~an effective amount of an acylhydroxamic acid derivative~~ a pharmaceutical composition according to claim 1, wherein said compound ~~which derivative~~ is a substantially chirally pure (R)-isomer, a substantially chirally pure (S)-isomer, or a mixture thereof.

23. (Currently amended) A method of treating an inflammatory or an autoimmune disease in a mammal ~~a disease selected from the group consisting of inflammatory disease and/or autoimmune disease~~, which comprises administering ~~thereto an effective amount of~~ a ~~compound~~ pharmaceutical composition according to claim 1, ~~which~~ wherein said compound is a substantially chirally pure (R)-isomer, a substantially chirally pure (S)-isomer, or a mixture thereof.

24. (Currently amended) ~~A~~ The method according to claim 23 wherein the disease is ~~at least one member selected from the group of~~ arthritis, rheumatoid arthritis, inflammatory bowel disease, Crohn's disease, aphthous ulcers, cachexia, graft versus host disease, asthma, chronic obstructive pulmonary disease ~~COPD~~, psoriasis, atopic dermatitis,

~~Lupus~~lupus, adult respiratory distress syndrome, ~~and~~ or acquired immune deficiency syndrome.

25. (Currently amended) A method of treating cancer in a mammal which comprises administering thereto ~~an effective amount of a compound~~ pharmaceutical composition according to claim 1, ~~which~~ wherein said compound is a substantially chirally pure (R)-isomer, a substantially chirally pure (S)-isomer, or a mixture thereof.

26. (Currently amended) A method of ~~treating~~ reducing angiogenesis ~~undesirable angiogenesis~~ in a mammal which comprises administering thereto ~~an effective amount of~~ a ~~compound~~ pharmaceutical composition according to claim 1, ~~which~~ wherein said compound is a substantially chirally pure (R)-isomer, a substantially chirally pure (S)-isomer, or a mixture thereof.

27. (Currently amended) A method of inhibiting the levels of phosphodiesterases type IV ~~or PDE 4~~ in a mammal which comprises administering thereto ~~an effective amount of an acylhydroxamic acid derivative~~ a pharmaceutical composition according to claim 1, ~~which derivative~~ wherein said compound is a substantially chirally pure (R)-isomer, a substantially chirally pure (S)-isomer, or a mixture thereof.

Claims 28-29. Cancelled.

30. The pharmaceutical composition ~~comprising a quantity of an acylhydroxamic acid derivative according to~~ of claim 5, ~~which derivative~~wherein said compound is a substantially chirally pure (R)-isomer, a substantially chirally pure (S)-isomer, or a mixture thereof, ~~sufficient upon administration in a single or multiple dose regimen to reduce or inhibit~~ wherein the composition is useful for reducing or inhibiting the levels of TNFα, PDE 4 or a matrix metalloproteinase in a mammal ~~in combination with a carrier~~.

31. Cancelled.

32. (Currently amended) A method of reducing or inhibiting the ~~undesirable~~ levels of TNFα in a mammal which comprises administering thereto ~~an effective amount of an acylhydroxamic acid derivative~~ a pharmaceutical composition according to claim 5, ~~which derivative~~ wherein said compound is a substantially chirally pure (R)-isomer, a substantially chirally pure (S)-isomer, or a mixture thereof.

33. (Currently amended) A method of inhibiting the ~~undesirable~~ levels of matrix metalloproteinases in a mammal which comprises administering thereto ~~an effective amount of an acylhydroxamic acid derivative~~ a pharmaceutical composition according to claim 5, ~~which derivative~~ wherein said compound is a substantially chirally pure (R)-isomer, a substantially chirally pure (S)-isomer, or a mixture thereof.

34. (Currently amended) A method of treating an inflammatory disease or an autoimmune disease in a mammal ~~a disease selected from the group consisting of inflammatory disease and or autoimmune disease~~, which comprises administering thereto ~~an effective amount of~~ a ~~compound~~ composition according to claim 5, ~~which~~ wherein said compound is a substantially chirally pure (R)-isomer, a substantially chirally pure (S)-isomer, or a mixture thereof.

35. (Currently amended) ~~A~~ The method according to claim 34, wherein the disease is ~~at least one member selected from the group consisting of~~ arthritis, rheumatoid arthritis, inflammatory bowel disease, Crohn's disease, aphthous ulcers, cachexia, graft versus host disease, asthma, chronic obstructive pulmonary disease ~~COPD~~, psoriasis, stopic dermatitis, ~~Lupus~~, adult respiratory distress syndrome, ~~and~~ or acquired immune deficiency syndrome.

36. (Currently amended) A method of treating cancer in a mammal which comprises administering thereto ~~, an effective amount of a compound~~ a pharmaceutical composition according to claim 5, ~~which~~wherein said compound is a substantially chirally pure (R)-isomer, a substantially chirally pure (S)-isomer, or a mixture thereof.

37. (Currently amended) A method of ~~treating~~ reducing angiogenesis ~~undesirable angiogenesis~~ in a mammal which comprises administering thereto ~~an effective amount of a compound~~ a pharmaceutical composition according to claim 5, ~~which~~ wherein said compound is a substantially chirally pure (R)-isomer, a substantially chirally pure (S)-isomer, or a mixture thereof.

38. (Currently amended) A method of inhibiting the ~~undesirable~~ levels of phosphodiesterase type IV in a mammal which comprises administering thereto ~~an effective amount of an acylhydroxamic acid derivative~~ a pharmaceutical composition according to

claim 5, ~~which derivative~~ wherein said compound is a substantially chirally pure (R)-isomer, a substantially chirally pure (S)-isomer, or a mixture thereof.

39. (Currently amended) A method of treating dermal diseases in a mammal which comprises administering thereto ~~an effective amount of an acylhydroxamic acid derivative~~ a pharmaceutical composition according to claim 5, ~~which derivative~~ wherein said compound is a substantially chirally pure (R)-isomer, a substantially chirally pure (S)-isomer, or a mixture thereof.

Claim 40. Cancelled.